

REMARKS

Claims 12-18 and 39 are currently pending in this application. Claim 39 is being amended herewith. Applicants are canceling Claims 12 and 17 herewith. Support for these amendment can be found generally throughout the specification. Following entry of the foregoing amendments, Claims 13-16, 18 and 39 will be pending. Applicants respectfully request further examination of those claims.

The Office Action:

The rejection questions the data in Table 2. Claims 39, 12 and 17 were rejected under 35 U.S.C. §103(a) as being obvious and unpatentable over EntreMed Overview and Attala et al. Applicants respectfully traverse the foregoing rejection. Claims 14-16 and 18 were allowed. were not rejected on the basis of any prior art.

Data in the Specification:

The rejection requests a clarification of the meaning of "R" in Table 2. However, applicants amended Table 2 in the prior response. Therefore, there is no longer an "R" in the headings of Table 2.

The rejection also questions the data regarding the IC₅₀ for 16-substituted compounds. The data shown in Table 2 is correct. The significance of the data is not that 16-substituted compounds are more active, but that they are metabolized more slowly to a less desirable form, and, therefore, have a longer time to be active.

Rejection under 35 U.S.C. § 103:

Claims 39, 12 and 17 were rejected under 35 U.S.C. §103(a) as being obvious and unpatentable over EntreMed Overview and Attala et al. The rejection states that the references teach the method of inhibiting angiogenesis by 2-methoxyestradiol. The rejection further states that when the claimed compound are substituted at the 16-position with Me and Et, they are considered homologues having similar properties to 2-methoxyestradiol and are therefore considered *prima facie* obvious. Applicants respectfully disagree.

Applicants submit that in the art of estradiols is highly unpredictable. The change of a single substituent from one ring position to another ring position can change the properties of the compound from being antiangiogenic to carcinogenic. Therefore, applicants disagree that the properties of homologues of 2-methoxyestradiol are expected to be the same as that of 2-methoxyestradiol. Nevertheless, in the interest of advancing prosecution of this case, applicants are amending Claims 39 and canceling claims 12 and 17, without prejudice, to provide that when one of R_{h1} or R_{h2} is H, the other of R_{h1} or R_{h2} is not Me or Et. Applicants submit that these amendment overcome the alleged *prima facie* obviousness of Claim 39. The rejection of Claims 12 and 17 is moot. Accordingly, applicants submit that Claim 39 is now allowable.

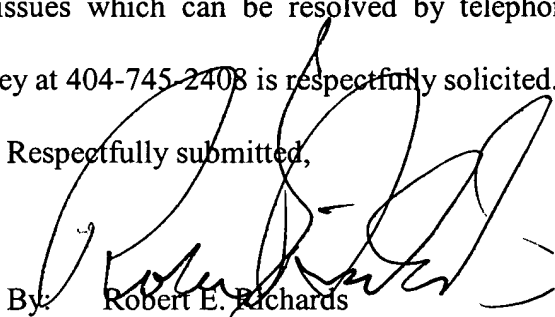
Allowed Claims:

Claims 14-16 and 18 were allowed in the Office Action. Applicants submit that the allowed claims should also include Claim 13, since the Office Action states that the prior art of record does not teach or fairly suggest R_{h1} or R_{h2} to include n-Pr, which is the subject of Claim 13. Also, the Office Action should properly states under the “Allowable Subject Matter” section that R_{h1} and R_{h2} are not both H.

Conclusion:

In view of the foregoing amendments and remarks, Applicants respectfully submit that Claims 13-16, 18 and 39 are in condition for allowance. Such action is respectfully requested. If there are informalities remaining in the application which may be corrected by Examiner's Amendment, or there are any other issues which can be resolved by telephone interview, a telephone call to the undersigned attorney at 404-745-2408 is respectfully solicited.

Respectfully submitted,

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